

Pleomorphic and Widespread Lesions of Phaeohyphomycosis in a Leprosy Patient on Corticosteroid

Sir,
Pheohyphomycosis is a rare fungal infection caused by brown-pigmented (phaeoid) or dematiaceous fungi.^[1] It usually presents as a localized subcutaneous cyst or abscess. Rarely verrucous plaques and pustules can occur in phaeohyphomycosis.^[2] Pleomorphic and widespread lesions in a single patient are rare and is usually seen in immunocompromised cases. Corticosteroids, used for control of reaction in leprosy patients, lead to immunosuppression. Here we report widespread lesions of phaeohyphomycosis with varied morphology in a leprosy patient on corticosteroid who responded to oral itraconazole.

A 62-year-old male farmer, who was on treatment for Borderline Hansen and type-1 lepra reaction for six months (multibacillary multidrug therapy and oral prednisolone 20 mg–40 mg), presented with multiple skin lesions of two months duration. He denied history of trauma prior to the development of lesions. Dermatological examination revealed different types of skin lesions that is subcutaneous nodules, cysts, abscesses, and pustules. Dorsum of right hand showing subcutaneous soft cystic swellings of size ranging from 0.5×1 cm² to 1.8×3 cm² arranged in a linear distribution [Figure 1a and b]. Similarly, on ring finger of left hand, there were pustular lesions and verrucous plaques. On the elbows and ankles, there were multiple small verrucous plaques [Figure 2a and b]. Based on the morphology, atypical mycobacteria, phaeohyphomycosis, and sporotrichosis were considered as differential diagnoses. There was no other systemic involvement. Routine laboratory investigations were normal and serological

screening for hepatitis B, hepatitis C, and human immunodeficiency virus were negative. FNAC, ECG, ultrasonography of abdomen, chest X-ray, and CECT were normal. Biopsy from verrucous plaques from right elbow revealed hyperkeratosis, and dense inflammatory infiltrates in the dermis [Figure 3a and b]. Staining with Periodic Acid Schiff (PAS) and Gomori-Methanamine Silver (GMS) showed plenty of pigmented fungal hyphae, pseudo hyphae and spores [Figure 4a and b]. Staining for AFB (Acid Fast Bacilli) was negative. KOH mount from the content of cyst revealed pseudo-hyphal fragments and yeast like forms on calcofluor white examination under UV light. Fungal culture of aspirate and tissue yielded non sporulating black mould in Sabouraud's dextrose agar media [Figure 5a and b]. A final diagnosis of widespread pheohyphomycosis was made. The patient was started on oral itraconazole 200 mg twice daily. Two months after, the lesions completely resolved [Figure 6]. He continued treatment for another two months. There was no recurrence after 6 months of follow up.

Phaeohyphomycosis is a rare fungal infection caused by dematiaceous fungi.^[1] More than 100 species have been implicated as causative agents, of which the most common are *Exophiala*, *Alternaria*, *Bipolaris*, *Curvularia*, and *Wangiella*.^[2] Subcutaneous phaeohyphomycosis appears to be increasing in recent years as the number of increases in immunocompromised cases. This may be due to increase use of corticosteroids, immunosuppressive drugs, and increased prevalence of AIDS. Other risk factors are found to be neutropenia, malignancy, and bone marrow transplant.

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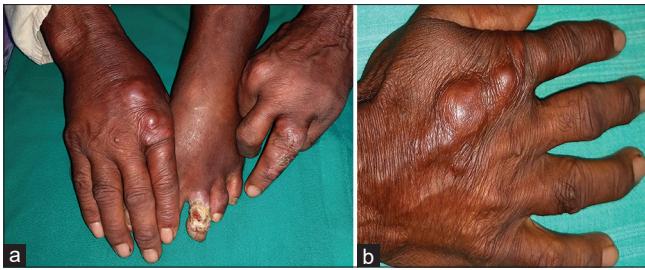


Figure 1: (a) Varied morphology like subcutaneous nodules, cysts, abscesses and pustules. (b) Cystic swellings in a linear distribution over dorsum of right hand

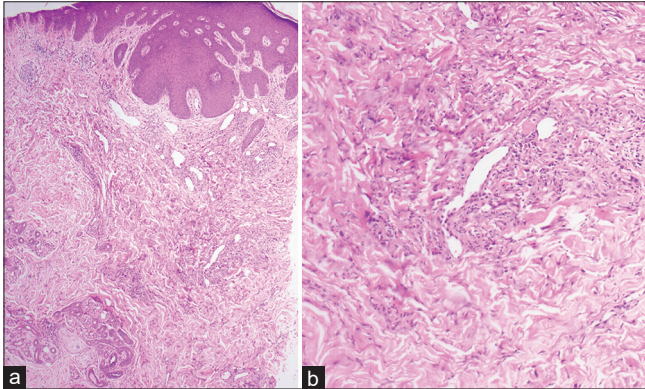


Figure 3: (a) Scanner view showing hyperkeratosis and dense inflammatory infiltrate in the dermis from verrucous plaque (H and E 40×). (b) High power view showing lympho-plasmocytic infiltrate in dermis (H and E 100×)

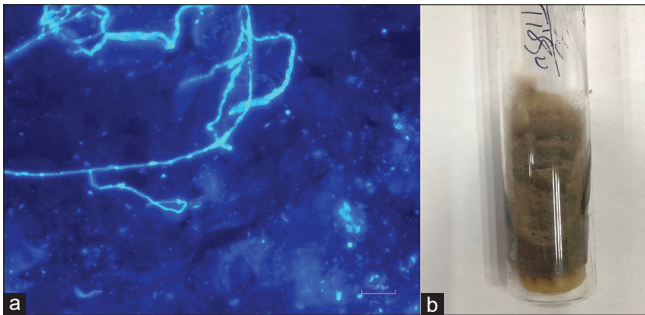


Figure 5: (a) KOH mount from the content revealed pseudo-hyphal fragments & yeast like forms on calcofluor white examination at 40× magnification under UV light. (b) Non sporulating black mould in Sabouraud's dextrose agar media

The climate ranges from tropical to temperate in India, and the disease has been reported from North to South, except for the Western and Eastern regions of the country.^[3] Our case was from eastern part of India. Table 1 summarises widespread phaeohyphomycosis cases reported from different zones of India.

Co-occurrence of phaeohyphomycosis and Hansen disease has been rarely reported. Kar *et al.* reported solitary lesions over extremities in a Hansen patient.^[11] Similarly, Teixeira *et al.* described subcutaneous cystic lesions over feet in a leprosy patient who was on long-term corticosteroid.^[12] Hence, the prolonged use of corticosteroid for control of reaction can cause immunosuppression resulting increased



Figure 2: (a) Verrucous plaques over elbow (b) Verrucous plaques over ankle

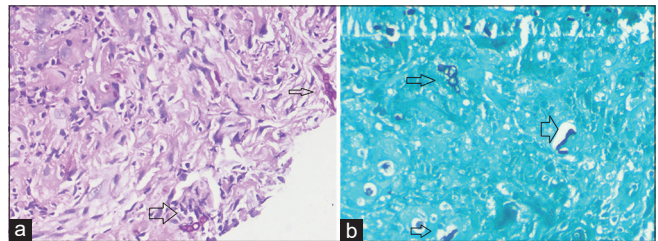


Figure 4: (a) Periodic acid Schiff showing pigmented fungal hyphae, pseudo-hyphae and spores. (b) Gomori-methanamine silver (GMS) staining showing fungal hyphae



Figure 6: Significant improvement of lesions 2 month after Itraconazole monotherapy

frequency of widespread fungal infection. Similar situation may be the cause of multiple site involvement in our case.

Phaeohyphomycosis can present as superficial, cutaneous, subcutaneous, and visceral forms. Subcutaneous infection causes phaeohyphomycotic cyst usually over the extremities. Varied clinical presentations include papules, nodules, verrucous, hyperkeratotic, or ulcerated plaques, cysts, abscesses, pyogenic granuloma, nonhealing ulcers, or sinuses.^[2] Four different types of morphology such as subcutaneous nodules and cysts, wart like hyperkeratotic

Table 1: Case reports of widespread phaeohyphomycosis reported from different parts of India with their outcome

| Author | Patient Details | Geographic area | Immune Status | Clinical features | Systemic Involvement | Investigations | Treatment outcome |
|--|-----------------|-----------------|--|--|--|--|--|
| Khader A <i>et al.</i> ^[4] | 38-year Female | Kerala | Nephrotic syndrome on corticosteroid and cyclosporine for 8 months | Pyogenic granuloma-like nodules, dermatophytosis-like plaque, and subcutaneous cysts in upper and lower extremities | No | Biopsy - black yeasts resembling sclerotic bodies, Culture - irregular, velvety, grey colonies of <i>Cladophialophora bantiana</i> | Successfully treated with itraconazole 100 mg twice daily for 2 months |
| Rajendran C <i>et al.</i> ^[5] | 12-year Female | Uttar Pradesh | Immunocompromised | Verrucous, well-defined plaques encompassing phaeohyphomycotic lesions on her face, chest, arms and thighs | Only left axillary node involved No systemic symptoms | Biopsy-Demonstrating pigmented fungal elements of the left axillary node Culture-Exophiala spinifera | Successfully treated with itraconazole 100 mg twice daily for 1.5 months |
| Radhakrishnan D <i>et al.</i> ^[6] | 20-year female | Tamilnadu | Cirrhosis | Non-healing ulcers, base was covered with unhealthy black granulation tissue and foul-smelling pus over her face, body, arms, and legs | pallor, anasarca, jaundice, generalized lymphadenopathy | Biopsy- non-cascating granulomatous lesion KOH-septate dematiaceous hyphal elements and pseudohyphae Culture-Exophiala spinifera | Ketoconazole 200 mg Expired due to liver failure |
| Chander R <i>et al.</i> ^[7] | 8-year Boy | North India | Immunocompromised | Brownish, round to oval, crusted plaques with multiple satellite lesions studded with black dots over the extremities, face and trunk | No | Culture-Exophiala spinifera FNAC -Budding yeast cells. | Resistant to itraconazole 200 mg 8 weeks and terbinafine 125 mg for 6 weeks and lost to follow up. |
| Vishal G. Mudholkar <i>et al.</i> ^[8] | 6-year Male | Maharashtra | Immunocompromised | Disseminated ulcerated fungating masses on his face, arms, thighs, and chest | No | Biopsy- Granulomatous infiltrates, neutrophilic abscess and thick-walled pigmented fungal spores on special stains were seen., Culture-Exophiala spinifera KOH- preparations from scrapings were negative for fungal hyphae or yeast cells Skin biopsy- many yeast-like cells and septate hyphae with brown-colored walls in the epidermis Culture-Exophiala jeanslemei | Itraconazole 100 mg once a day for 5 months and surgical excision of residual lesion |
| Ramprasad A <i>et al.</i> ^[9] | 30-year male | North India | Immunocompromised | Recurrent ulcerative-nodular, verrucous swellings over face, trunk and back | No | Culture-Exophiala jeanslemei | 75% resolution by amphotericin B and flucytosine, followed by treatment with itraconazole (200 mg twice daily) and terbinafine (250 mg once daily) |

Contd...

Table 1: Contd...

| Author | Patient Details | Geographic area | Immune Status | Clinical features | Systemic Involvement | Investigations | Treatment outcome |
|---|----------------------|-----------------|--|--|----------------------|---|---|
| Koppada R <i>et al.</i> ^[10] | 45-year Female | Vijayawadae | Immunocompromised Taking antiretroviral therapy | Tender nodular lesions draining pus on face, hands, axilla, groin & labia majora | No | KOH-brown coloured hyphae with septations indicating phaeoid fungi Culture (LPCB)-Exserohilum species | Itraconazole 200mg BD and Terbinafine 250mg BD, healing of pustular lesions in two weeks. |
| Our case | 62 year/ male farmer | Eastern India | Leprosy on corticosteroid | Subcutaneous cyst, lobulated mass, pustule, verrucous plaques over bilateral hands, feet, Elbows, and ankles | No | Biopsy with PAS &- GMS- plenty of pigmented fungal hyphae, pseudo-hyphae and spores KOH-pseudo-hyphal fragments & yeast like forms on calcofluor white under UV light SDA-non sporulating black mould | Successfully treated with Itraconazole for 2 months and continued for another 2 months. |

plaques and pustular lesions coexisted in our patient. Co-occurrence of similar morphological types has not been described previously, although combination of warty lesions and cystic lesions are described in disseminated phaeohyphomycosis by Revankar *et al.*^[13] There is only one case report of phaeohyphomycosis presenting as innocuous pustule.^[2] Melanin is a virulence factor that acts as an antioxidant against oxidative bursts produced by phagocytes resulting dissemination of the disease. Although there were no systemic features in our patient, widespread lesions over hands, foot, and ankle could be due to haematological or lymphatic spread of the fungus on the background of immunosuppression or auto-inoculation.

The diagnosis is mainly through demonstration of fungus in histopathology and culture. Special staining techniques like GMS and PAS identifies the organism. Our patient had similar findings. Treatment of subcutaneous and disseminated phaeohyphomycosis includes surgical excision and anti-fungal therapy. Itraconazole 200 mg twice daily for 4–6 months has the best record. Our patient responded very well to itraconazole within 2 months. Physicians should consider cutaneous phaeohyphomycosis in the differential diagnosis of plaques, nodules, pustules, and cysts in the skin, especially in the setting of immunosuppression even in Hansen patients. Hence, early diagnosis and early identification of fungus followed by appropriate management may prevent systemic dissemination and lead to a favourable outcome.

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Conflicts of interest

There are no conflicts of interest.

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